

CLAIMS:

1. A polypeptide comprising an amino acid sequence comprising two or more receptor binding residues substantially defined by structural coordinates of amino acids Met 6, Arg 8, Lys13, Gln17, Asp31, Val33, Pro46, Val55, Gly92, Gly93, Gln103, Ser105 and Tyr147 of SEQ ID NO: 2 as set forth in Tables II or III, and said polypeptide capable of binding IL-1 receptor (IL-1R).
2. A polypeptide according to claim 1, wherein said receptor binding residues have a root mean square deviation from the structural coordinates set forth in Tables II or III of said amino acids Met 6, Arg 8, Lys13, Gln17, Asp31, Val33, Pro46, Tyr147, Val55, Gly92, Gly93, Gln103 and Ser105 of not more than 5 Angstroms.
3. A polypeptide according to claim 1, wherein said receptor binding residues have a root mean square deviation from the structural coordinates set forth in Tables II or III of said amino acids Met 6, Arg 8, Lys13, Gln17, Asp31, Val33, Pro46, Tyr147, Val55, Gly92, Gly93, Gln103 and Ser105 of not more than 2 Angstroms.
4. A polypeptide according to claim 1, wherein the polypeptide includes a basic amino acid residue at a position corresponding to position 145 of SEQ ID NO: 2.
5. A polypeptide according to claim 4, wherein the basic residue at the position corresponding to position 145 of SEQ ID NO: 2 is a lysine.
6. A polypeptide according to claim 1, wherein the portion of the polypeptide outside of the IL-1R binding region has a three-dimensional conformation substantially different from that of IL-1 Hy2 of SEQ ID NO: 2.
7. A polypeptide according to claim 1, that is less than 85% identical over its entire length to SEQ ID NO: 2.
8. A composition comprising a polypeptide according to claim 1.

9. A computer comprising a memory containing a three dimensional representation of IL-1 Hy2 or of a portion of IL-1 Hy2 that includes the IL-1R binding region of IL-1 Hy2.

10. A computer according to claim 9, wherein the three dimensional representation is substantially defined by structural coordinates of IL-1 Hy2 amino acids Met 6, Arg 8, Lys13, Gln17, Asp31, Val33, Pro46, Val55, Gly92, Gly93, Gln103, Ser105 and Tyr147 of SEQ ID NO: 2 as set forth in Tables II or III.

11. A computer according to claim 9, wherein the IL-1R binding region has a root mean square deviation from the structural coordinates set forth in Tables II or III of said amino acids Met 6, Arg 8, Lys13, Gln17, Asp31, Val33, Pro46, Val55, Gly92, Gly93, Gln103, Ser105 and Tyr147 of not more than 5 Angstroms.

12. A computer according to claim 9, comprising a machine readable data storage medium, a data storage material coded with machine readable data, said data including said three dimensional representation.

15 13. A machine readable data storage medium containing machine readable data, said data including a three dimensional representation of IL-1 Hy2 or of a portion of IL-1 Hy2 that includes the IL-1R binding region of IL-1 Hy2.

14. A machine readable data storage medium according to claim 13 wherein the three dimensional representation is substantially defined by structural coordinates of amino acids Met 6, Arg 8, Lys13, Gln17, Asp31, Val33, Pro46, Val55, Gly92, Gly93, Gln103, Ser105 and Tyr147 of SEQ ID NO: 2 as set forth in Tables II or III.

15. A method for identifying a potential modulator of IL-1 Hy2 biological activity, the method comprising steps of:

- (a) using a three-dimensional structure of IL-1 Hy2 substantially defined by structural coordinates of two or more IL-1 Hy2 (SEQ ID NO: 2) amino acids Met 6, Arg 8, Lys13, Gln17, Asp31, Val33, Pro46, Val55, Gly92, Gly93, Gln103, Ser105, Lys145 and Tyr147 as set forth in Tables II or III to design or select a potential modulator of IL-1 Hy2 biological activity;
- (b) contacting said potential modulator with IL-1 Hy2 in the presence of IL-1R to test the ability of said potential modulator to modulate the interaction between IL-1 Hy2 and IL-1R.

16. The method of claim 15 wherein in step (a) the potential modulator is selected by screening modulators using a computer for interaction with the three-dimensional structure of IL-1 Hy2.

17. The method of claim 15 further comprising the step of contacting said potential modulator with an IL-1 Hy2 mutant in the presence of IL-1R to test the ability of said potential modulator to modulate the interaction between the IL-1 Hy2 mutant and IL-1R, said IL-1 Hy2 mutant exhibiting reduced binding to IL-1R compared to wild type IL-1 Hy2 of SEQ ID NO: 2.

18. A method for identifying a potential modulator of IL-1 Hy2 biological activity, the method comprising steps of:

- (a) using a three-dimensional structure of IL-1 Hy2 substantially defined by structural coordinates of two or more IL-1 Hy2 (SEQ ID NO: 2) amino acids Met 6, Arg 8, Lys13, Gln17, Asp31, Val33, Pro46, Tyr147, Val55, Gly92, Gly93, Gln103, Ser105, Lys145 and Tyr147 as set forth in Tables II or III to design or select a potential modulator of IL-1 Hy2 biological activity;
- (b) contacting said potential modulator with a IL-1 Hy2 mutant in the presence of IL-1R to test the ability of said potential modulator to modulate the interaction between IL-1 Hy2 and IL-1R, said IL-1 Hy2 mutant exhibiting reduced binding to IL-1R compared to wild type IL-1 Hy2 of SEQ ID NO: 2.

19. The method of claim 17 or 18 wherein said mutants comprise at least one modification wherein an amino acid residue selected from the group consisting of Met 6, Arg 8, Lys13, Gln17, Asp31, Val33, Pro46, Val55, Gly92, Gly93, Gln103, Ser105, Lys145 and Tyr147 replaced with a different amino acid, and wherein said IL-1 Hy2 polypeptide variant
5 exhibits decreased binding to IL-1R compared to IL-1 Hy2 of SEQ ID NO: 2.

20. A method of treating a pathological condition characterized by aberrant expression or activity of IL-1 Hy2, comprising administering to a patient a therapeutically effective amount of a non-peptidyl compound that is a biological modulator of IL-1 Hy2 interaction with IL-1R, said compound containing one or more moieties that mimic one or
10 more of the IL-1 Hy2 amino acids of SEQ ID NO: 2 selected from the group consisting of Met 6, Arg 8, Lys13, Gln17, Asp31, Val33, Pro46, Val55, Gly92, Gly93, Gln103, Ser105, Lys145 and Tyr147 and as set forth in Tables II or III.

21. A method of treating a pathological condition characterized by aberrant expression or activity of IL-1R, comprising administering to a patient a therapeutically
15 effective amount of a polypeptide of any one of claims 1 through 7.

22. The method of claim 21 wherein the pathological condition is psoriasis.

23. An IL-1 Hy2 polypeptide variant comprising at least one modification wherein an amino acid residue selected from the group consisting of Met 6, Arg 8, Lys13, Gln17, Asp31, Val33, Pro46, Val55, Gly92, Gly93, Gln103, Ser105, Lys145 and Tyr147 is
20 replaced with a different amino acid, and wherein said IL-1 Hy2 polypeptide variant exhibits increased binding to IL-1R compared to IL-1 Hy2 of SEQ ID NO: 2.

24. An IL-1 Hy2 polypeptide variant comprising at least one modification wherein an amino acid residue selected from the group consisting of Met 6, Arg 8, Lys13, Gln17, Asp31, Val33, Pro46, Val55, Gly92, Gly93, Gln103, Ser105, Lys145 and Tyr147 is replaced with a different amino acid, and wherein said IL-1 Hy2 polypeptide variant exhibits
5 decreased binding to IL-1R compared to IL-1 Hy2 of SEQ ID NO: 2.

25. A polypeptide of claim 23 or 24 that is less than 85% identical over its entire length to SEQ ID NO: 2.

26. A polypeptide of claim 23 or 24, wherein the amino acid is replaced with a conservative substitution.

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